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Trip Report: Leukemia Project, UA Cleanup Workers
20-26 June, 1999

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Introduction: This was a major site visit by an extensive NCI-IPSN team to review accomplishments and preparations for the completion of the work of the final 6 months of funding (July-December, '99). At issue were the completion of the final report on Phase I tasks, and scheduling its review by the originating working groups, the decision about Phase II, and any modification of the 1995 research protocol for Phase II.

The NCI delegation was led by Dr Masnyk, director of the NCI Chernobyl Projects, accompanied by Dr Bouville, Dr Luckyanov, and myself, and by consultants made available for the project through the support services contract with Columbia University: Drs Burch, Howe, McFee, Reiss, and Zablotska (Ukrainian physician studying epidemiology with Dr Howe). The IPSN delegation consisted of Dr Hubert and Margot Tirmarche. A representative of the Department of Energy, Mr Fountos, accompanied the NCI delegation.

Six-Month Extension: In his letter of 5 May Dr Romanenko had outlined plans for the final 6 months. Their discussion clarified the actual requirements for completing Phase I and led to a better understanding of the schedule for preparing and reviewing the final report on Phase I and for developing a position on Phase II.

Selection of the Six Oblasts: Although an initial selection had been made in 1995 when the research protocol was prepared, the finding, in the recent diagnostic review, that records of the retrospective period were inadequate in 2 oblasts, necessitated their replacement with 2 other oblasts. Medical record reviews were being conducted; one replacement had been accepted and work on another was almost complete. We went back and forth over the criteria that the leukemia records of the cleanup workers should satisfy in order to qualify an oblast for inclusion, but without taking a formal position. My own suggestion was to frame criteria in terms of the proportion of the leukemia cases of the retrospective period with slides, tissue, and medical records for review, and to avoid the necessity for an actual study of the diagnostic materials. The selection of the substitute oblasts was a task being handled by the hematology and the epidemiology groups.

Phase II. Discussion quickly turned to Phase II, whether it would be recommended and what its content would be. Dr Bebeszko wanted to be sure that lymphoma was retained. Dr Howe outlined the reasons why lymphoma might not be an acceptable cancer to study in Phase II. Others favored discussion of the pros and cons of a review of Phase II objectives and methods, but it was possible to limit the discussion largely to Phase I, its completion, the preparation of a

summary report, and scheduling the steps that would need to be taken in the final 6 months. Hope was expressed that Phase I could be brought to a quick conclusion so that the final report could be evaluated promptly and attention turned to deciding about Phase II, including any modifications of the 1995 protocol.

The *molecular studies* proposed in the 1995 protocol were also defended by Dr Bebeshko. The Phase I task of assembling the high-dose cohort for these studies was incomplete and doubt was expressed that a sample of sufficient size could be assembled. On the other hand, there was evidence that the Ministry of Internal Affairs would release its file on cleanup workers, and that file was believed to contain additional workers with relatively high doses. Also, the eligibility criteria for the high-dose sub-cohort were not those set for the main cohort. With only about 1,000 in hand it had thus far been difficult to obtain a cohort of 2,500 with doses of 0.5 or more GY, and there also was little evidence of the excess leukemia among the workers that would encourage the studies envisaged in the protocol.

Work on Specific Tasks: Pilot work on the *ascertainment of leukemia* indicated that the most reliable and inclusive source would be the hematology dispensaries at the oblast level. Diagnoses entered into the National Chernobyl Registry would be worth scanning for leukemia and a variety of related diagnoses, as was also true of the geographically incomplete Ukrainian Cancer Registry. At best, however, these sources could supplement in only a minor way the ascertainment based on the hematology dispensaries at the oblast level. I advocated that CLL not be neglected in collecting cases, as some of them might turn out to be other forms of leukemia and the absence of a dose relationship with CLL, in the presence of such relationships with other forms of leukemia, could be supportive.

The *diagnostic review* conducted in January seemed to me to require no supplementary work based on other, smaller, and less formal evaluations. There was, however, some opinion favoring an integration of all available data of this kind in Ukraine, although the protocol does not require it. I suggested that Dr Finch could be expected to provide a draft on this task for the final report and that it could be ready for review soon. Dr Klimenko was concerned that the records of the cleanup workers might differ from those of the general population that had been sampled for the diagnostic review.

The *dosimetry group*, with considerable assistance from outside groups interested in the problem, was close to performing its planned comparisons of dose estimates made by the several methods available, none of which could produce estimates for all the subcohort and all the cases of interest. The EPR appeared to have been accepted as the "gold standard" and the task would be to correlate the estimates of each of the other methods with the EPR estimates for the same subjects. The dosimetry group was waiting for the FISH results to be made available for about 50 subjects, and that work, initially delayed by equipment and supply problems, was now well under way with technical assistance from Dr McFee. It was planned that individual dose estimates would be accompanied by ranges of uncertainty. Dr Bouville thought the dosimetry group would complete its tasks by the end of September.

The *ascertainment of hematologic diseases other than leukemia and lymphoma* had been partially investigated and would have to be re-worked by the epidemiology group to satisfy the Phase I requirement.

The *epidemiologic field work in Dniepropetrovsk*, the test oblast, was essentially finished and had produced estimates of the frequency with which workers had not been seen in the polyclinics for several years, the ease of locating representative workers, their willingness to be interviewed, and their willingness to give blood. Two estimates were cited: 31 of 47 approached (67 %) could be interviewed, and 11 of 31 requested (35%) had given blood.

Collecting, Processing, and Archiving Samples of Blood, Marrow, and Teeth: These activities had been well organized but the bloods had not been processed as prescribed in protocol Appendix 3. A catalog system was needed for bloods; one was available for the tooth archive.

Preparation on Report on Phase I: Dr Romanenko said that Dr Pyatak would be the editor. I suggested that the report consist of an introduction, and in their sequence, the consolidated summary of each task, followed by a brief account of its investigation, amplified by such statements or appendices as seemed necessary to those who did the work. I promised to write Dr Padauk along the lines of our discussion. I also indicated that NCI staff and consultants were available to assist in the preparation or the review of draft material. I expressed surprise that only Dr Chumak had provided draft material for this meeting, as I had been told of an agreement in March that draft material should be available for this meeting on all the tasks. I repeated that NCI staff and consultants were available to assist in the preparation or the review of draft material. I urged that no new work, not explicitly called for in the research protocol, be added to any existing Task, and that only what was required according to the protocol be represented in these write-ups, with the exception of dosimetry where the work had gone beyond what had been foreseen in the research protocol.

As we discussed the preparation of the report on Phase I it became clear that each group finishing a task would naturally consider how its results might affect the Phase II plan in the protocol of 1995. I reminded the group that the 1995 protocol called for the evaluation of Phase I and the modification and re-budgeting of phase II. In fact, the schedule in the protocol (para 5.2.9) provides for these activities to occupy the last several months of the projected 18-month period, now stretched to 24 months.

To stimulate discussion I suggested the following time-table:

July-September: Completion of outstanding tasks

Drafting task reports

Review of draft material

by 30 September Complete Draft Report

October Technical reviews of Phase I report by NCI, IPSN, and Radiation
Medicine Center

November **Formulation of protocol changes desired for Phase II**
Joint meeting in Washington of US and UA working groups that
authored the 1995 protocol, together with IPSN representatives

December **Decisions on protocol changes for Phase II**
A joint editorial group would make the necessary changes in
the 1995 research protocol
Submittal of revised Phase II research protocol to funding
agencies by 31 December, 1999